PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	Confirmation No.: 1891
Samir M. HANASH et al.	Art Unit: 1642
Application No.: 10/674,228	Examiner: Peter J. Reddig
Filed: September 29, 2003	Attorney Dkt. No.: 108140.00015

For: METHOD FOR IDENTIFICATION OF CELLULAR PROTEIN ANTIGENS AND PRESENCE OF ANTIBODIES TO SPECIFIC CELLULAR PROTEIN ANTIGENS IN SERUM

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December 3, 2008
Date
Marylee Scalzo

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Date: December 3, 2008

Sir:

In response to the Final Office Action mailed June 9, 2008, Applicant respectfully submits that the Office Action is both factually and legally incorrect, and hereby submits this Pre-Appeal Brief Request for Review. This request is not accompanied by an amendment to the currently pending claims, and is being filed with a Notice of Appeal.

Claims 1, 2, and 4 are pending in the subject application, with claim 1 being the sole independent claim. The outstanding Office Action is the sixth Office Action in this application. This application qualifies for Appeal.

The outstanding Office Action rejected claims 1, 2, and 4 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Hirsch et al. and Krska et al. Applicant respectfully traverses this rejection, and submits that it was made in error for at least the reasons set forth below.

Essential Elements are Not Disclosed by the Cited References

In the outstanding Office Action, the Examiner has cited references that do not disclose or suggest all of the claimed features.

Applicant respectfully submits that the cited references fail to disclose or suggest a method for identifying cellular protein antigens, ***to which a subject with cancer produces autoantibodies and a subject without cancer does not, without prior knowledge of the proteins being identified,*** said method ***consisting of***: (a) extracting proteins from a sample of cells; (b) separating the extracted proteins by two-dimensional electrophoresis; (c) transferring the proteins separated by two-dimensional electrophoresis to a membrane; (d) incubating the membrane with serum from a subject known to have the cancer; (e) detecting the proteins to which autoantibodies in the subject's serum have bound; and (f) comparing the proteins to which antibodies in the subject's serum sample bind to proteins to which antibodies in a control serum sample from a subject without cancer bind, ***wherein those proteins bound by antibodies in the serum from the subject with cancer but not the control serum from the subject without cancer are identified as cellular protein antigens to which a subject with cancer produces autoantibodies and a subject without cancer does not.***

Rejection over Hirsch et al. and Krska et al.

Hirsch et al. discloses a method for screening antibodies in serum samples from patients afflicted with Hodgkin's disease in which the serum proteins are first subjected to 1D gel electrophoresis and western blotting to identify a particular polypeptide. The samples are then used in 2D immunoblotting to further characterize the previously-identified polypeptide. The prior knowledge derived from the 1D electrophoresis is necessary for Hirsch et al. to perform all subsequent steps of the method disclosed therein, in which 2D immunoblotting is used to further characterize the peptide.

Applicant submits that one of ordinary skill in the art, having the disclosure of Hirsch et al. before him, would conclude that 2D western blots may only be interpreted by having *a priori* knowledge of the protein of interest derived from first performing 1D electrophoresis.

The presently-claimed invention provides a means, previously not available, for performing 2D western blots to discover proteins to which patients with cancer raise autoantibodies, where individuals without cancer do not, ***without prior knowledge of the proteins to be so identified.***

The outstanding rejections based on Hirsch et al. ignore the fact that Applicants' claims recite a method "consisting of" steps (a) through (f). It is well-settled that ***the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim.*** *See* MPEP 2111.03. Applicants submit that the method disclosed in Hirsch et al., in which an initial 1D electrophoresis must be performed to interpret the results of a subsequent 2D immunoblot, does not disclose or suggest the presently-claimed invention, in which a 2D immunoblot is used to discover proteins to which patients with cancer raise autoantibodies, where individuals without cancer do not, without prior knowledge of the proteins to be so identified.

One skilled in the art would not be motivated to modify the techniques disclosed in Hirsch et al. by eliminating the 1D electrophoresis step to arrive at the presently-claimed invention, and there is no suggestion in the prior art that such a modification would produce a useful result. In fact, Hirsch et al. discourages elimination of the 1D electrophoresis step. The legend to Figures 1A-C found at the foot of page 205 of Hirsch et al. states: "A polypeptide with a molecular weight of $65x10^3$ daltons gave a strong reaction in the one- (B,C) and two-dimensional (A) blots. ***Additional faint bands and spots reflect the usual background reaction.***" (Emphasis added.) Further, while it is apparent from Hirsch et al. that antibodies were produced for one protein, namely, P-65 in leukemia patients, Hirsch et al. first had to perform 1D PAGE and Western blotting to identify a protein to which only 17% of patients with cancer studied raise antibodies, and to which 2% of controls also have reactive antibodies. This lack of discrimination leads Hirsch et al. to conclude that "the relationship between antibodies to P-65 and HD is not clear" (p. 207, col. 1, lines 3-4).

These deficiencies of Hirsch et al. are not remedied by further combination with Krska et al., which is cited for disclosing a conventional method of 2D PAGE followed by western blotting analysis to detect antibodies bound to an antigen of interest, where the antibodies are transferred to a membrane.

The key difference between the presently-claimed invention and the cited references is that the combination of Krska et al. and Hirsch et al. requires prior knowledge of the protein of interest before Western blot patterns can be interpreted, whereas the presently claimed invention permits the discovery of proteins without prior knowledge of the proteins to be identified. Krska et al. does not disclose a method ***consisting of*** Applicants' steps (a) through (f), and does not provide any suggestion or motivation to modify the disclosure of primary reference Hirsch et al. to eliminate the 1D electrophoresis step to arrive at Applicants' presently claimed invention.

Applicants submit that the Office Action is improperly interpreting the claims in order to maintain the rejections based on Hirsch et al. and Krska et al. Specifically, the Office Action apparently continues to read the claims as being directed to a method "comprising" Applicants' claimed steps (a) through (f), rather than the presently-claimed methods which ***consist of*** Applicants' claimed steps (a) through (f).

Accordingly, in view of the above, the combination of Hirsch et al. and Krska et al. fails to disclose or suggest all the features of the presently-claimed methods, and nothing in their disclosures would lead one skilled in the art to modify them without the benefit of hindsight reconstruction based on Applicants' disclosure. Applicants therefore submit that The Office Action has failed to establish a *prima facie* case of obviousness for purposes of a rejection of claims 1, 2, and 4 under 35 U.S.C. § 103(a). As such, Applicant submits that claims 1, 2, and 4 are allowable over Hirsch et al. and Krska et al., and respectfully request that this rejection be withdrawn.

Conclusion

For all of the above reasons, a favorable decision and allowance of all pending claims are earnestly solicited.

In the event this paper is not considered to be timely filed, Applicant respectfully petitions for an appropriate extension of time. Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to counsel's Deposit Account No. 01-2300, **referencing Attorney Dkt. No. 108140.00015.**

Respectfully submitted,

Date: December 3, 2008

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Enclosures: Notice of Appeal (Form PTO/SB/31)
Pre-Appeal Brief Request for Review (Form PTO/SB/33)

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
108140.00015

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on 12/3/08

Signature

Typed or printed name Marylee Jenkins

Application Number	Filed
10/674,228	September 29, 2003

First Named Inventor
Samir M. HANASH

Art Unit	Examiner
1642	Peter J. Reddig

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 37,645
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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12/3/08
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NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [x] *Total of 1 forms are submitted.

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